State of New Hampshire
Cancer Cluster Investigation Protocol

NH DIVISION OF Public Health Services
Improving health, preventing disease, reducing costs for all
Department of Health and Human Services

Cancer Clusters: Background Information

The Centers for Disease Control and Prevention (CDC) defines a cancer cluster as a greater-than-expected number of cancers that occurs within a specific group of people, in geographic area over a defined period of time.[1] This definition can be broken down as follows:

- The observed number of cases of a cancer is higher than one would typically observe in a similar setting (e.g., a group of people with similar ages, gender and race).
- All of the cases involve the same type of cancer *or* different types of cancer that science has proven to have the same cause.
- The cancers are occurring in a carefully defined population. This may include factors such as age, gender, race or ethnicity.
- The boundaries for the area are carefully defined based on a perceived exposure.
- The time period over which the cases occurred is well defined.

Some cancer clusters occur simply by chance. In these situations, clusters are not the result of a single, external cause; instead, the cluster simply reflects coincidental spatial grouping among individuals who have been diagnosed with cancer. The smaller the number of cases the more likely this is to occur.

Other cancer clusters could be due to environmental exposure; however, cancer cluster investigations rarely link cancers with chemical exposures. It is important to understand that the majority of investigations that have found a link were related to occupational or drug-induced exposures of high doses in short time periods, rather than low-level environmental exposures.[2] For this reason, in the absence of a potential known cancer causing exposure, the CDC does not recommend that health departments conduct open-ended investigations to identify potential contaminants in communities.[1]

Cancer clusters may also reflect better access to health care. Residents from one geographic area may be more likely to be screened for cancer compared to residents from another area. In these situations, cancer clusters may exist because of certain cancers that are identified and treated but would have never become symptomatic (e.g., certain prostate or breast cancers). As such, these cancer clusters do not reflect a truly elevated cancer risk in a geographic area.

Finally, cancer clusters may be due to clustering of lifestyle behaviors. Tobacco use, regular physical activity, diet, and other behaviors strongly impact cancer risk. If residents in one geographic area are more likely to engage in unhealthy lifestyle behaviors, the cancer incidence rate for that area may be elevated compared to other areas.

[1] Centers for Disease Control and Prevention (CDC). Investigating Suspected Cancer Clusters and Responding to Community Concerns: Guidelines from CDC and the Council of State and Territorial Epidemiologists. Morbidity and Mortality Weekly Review September 27, 2013; 62(RR08); 1-14.
[2] Kingsley, BS, Schmeichel KL, Rubin, CH. An update on cancer cluster activities at the Centers for Disease Control and Prevention. Environmental Health Perspectives 2007; 115:1; 65-71.

Phases to Investigating a Cancer Cluster

This cancer cluster protocol parallels the cluster investigation guidelines published by the Centers for Disease Control and Prevention (CDC) in the September 2013 Morbidity and Mortality Weekly Report[3]. The protocol outlines four major steps and highlights key decision points involved in each step.

Phase I: Initial Contact and Response

In this phase the Division of Public Health Services (DPHS) collects information from the person reporting concerns (reporter) to determine whether the concerns warrant further follow-up.

1. **Person requesting/initiating an investigation reports case(s) through karen.paddleford@dhhs.nh.gov or 603-271-1568**

2. **Investigator conducts a literature review to obtain background information on:**
    a. Risk factors for the type of cancer(s) of concern (including environmental risk factors)
    b. Prevalence and distribution of type of cancer(s) of concern

3. **DPHS calls reporter within two business days of original inquiry to:**
    a. Verify reporter contact information
    b. Gather additional information from reporter including name, street address, zip code, preferred contact phone number, and email address
    c. Discuss specific cancer type(s) of concern
    d. Discuss geographic area in which cancer cases are observed: determine if reporter is concerned about rates in their zip code, or in a smaller area, such as their specific neighborhood or several streets
    e. Obtain information about specific cancer cases, including patient's last name and date of birth (if requester is aware of any), type of cancer and age at diagnosis in order to verify cancer diagnosis with the State Cancer Registry **(Note: if the reporter has this level of information, they may provide it directly; if they do not have the information, but have a relationship with the affected individual(s), the reporter will be informed that they may encourage the affected individual(s) to report their related case(s) directly to the State of New Hampshire using the dedicated email address or phone number provided in Phase I, step 1)**
    f. Record reporter's perceived environmental risk factors (if any) and determine if there is a known contaminant of concern or an occupational exposure. Make referrals where appropriate to the Department of Environmental Services, Environmental Health Program or the Occupational Health Program at the University of New Hampshire
    g. Inform reporter of DPHS's cancer cluster investigation protocol
    h. Discuss prospective timeline, inform reporter that depending on preliminary conclusions it may take several months to respond to their request
    i. Provide investigator's contact information and encourage reporter to contact investigator with any concerns or questions about the investigation process

4. **Investigator conducts review of New Hampshire State Cancer Registry (NHSCR) data to:**
    a. Verify that specific cases provided by requester (if any) represent actual cancer diagnoses
    b. Perform basic cancer analyses, if appropriate, using most recent five years of data. Analyses

[3] Centers for Disease Control and Prevention (CDC). Investigating Suspected Cancer Clusters and Responding to Community Concerns: Guidelines from CDC and the Council of State and Territorial Epidemiologists. Morbidity and Mortality Weekly Review September 27, 2013; 62(RR08); 1-14.

may include:

- Total number of cancers for area
- Distribution of cancer cases by type (SEER sites)
- Comparison of area distribution to another similar population (either county or state population)
- Area-specific incidence rates for comparison
- Age-adjusted rates for requested cancers
- Time trend of number and rates of specified cancer by year
- Comparison of area-specific incidence rates to rates for larger geographic regions: Zip code vs. county vs. New Hampshire vs. United States
- If requester is especially concerned about environmental hazards, rates for known associated cancers

5. **Investigator makes conclusion of:**

   - No cluster → No further investigation needed
   - Possible cluster → Need to conduct further analysis, proceed to next step

   Note: Although the conclusion is listed as the last step in Phase I, it can occur at an earlier point based on any combination of the following:

   - Information obtained from reporter
   - Findings of literature review
   - Findings of NHSCR review and basic analyses

   In the conclusion summary, the investigator comments about the following, as appropriate:

   - Cancer Type(s)
   - Frequency of cancer occurrence
   - Geographic occurrence
   - Number of cases
   - Sex distribution
   - Age distribution
   - Environmental concerns
   - Exposure experienced by the individual with the cancer of interest
   - Biological plausibility of reported exposure as a cause of cancer based on scientific literature about causes of reported cancer
   - Community contextual factors possibly influencing cancer concerns, including political activity, media coverage, and/or advocacy group involvement.

6. **DPHS publishes conclusion on State of New Hampshire DPHS website and captures these activities in an annual report.**

Phase II: Assessment

The purpose of this phase is to determine if the reported cancer concerns represent a true cancer cluster based on the presence of a statistically significant excess of cancer.

1. **Investigator establishes a standard set of criteria to help DPHS identify all cases that should be included in the cluster analyses including:**

   - Cancer type
   - Residence at the time of diagnosis
   - Year of diagnosis
   - Age at diagnosis
   - Sex

2. **Investigator conducts review of New Hampshire State Cancer Registry (NHSCR) data to:**

   a. Analyze trends in age at diagnosis for identified cancers
      i. Verify that average age of diagnosis occurs within the expected age group
      ii. Determine number of outliers (cases diagnosed at a much younger or older age than expected)
   b. Calculate expected number of cases based on cancer rate(s) in a similar comparison population
      i. Calculate appropriate population denominators for area under investigation
      ii. Calculate census-based estimates of the ratio of the area population to total NH population
   c. Compare the observed vs. expected number of cancer cases
      i. Determine if significant differences exist between local area and comparison population rates
      ii. Calculate 95% confidence intervals (CIs) for area-specific rates
      iii. Conduct test(s) to determine whether or not differences in area-specific rates and the state-level rate are statistically significant.
      iv. If area-specific rates are significantly higher than state rates, calculate age, race, and gender-specific incidence rates for the area under investigation
      v. Calculate standardized incidence ratios (SIRs) for cancers that are significantly elevated at the area-specific level compared to the state rate
   d. In instances where the population is large enough DPHS will calculate and compare age-adjusted incidence rates between the area under investigation and relevant comparison population

3. **Investigator convenes the Cancer Cluster Review Team (CCRT) with membership from the NH Department of Health and Human Services, the NH State Cancer Registry and other agencies (NH Department of Environmental Services, Centers for Disease Control and Prevention, and Environmental Protection Agency) as needed to make a recommendation on next steps considering the following:**

   - Are there enough cases and a large enough population for statistical stability?
   - Review confidence intervals to determine whether a significant SIR could be related to chance
   - Are there potentially environmental contaminants present which are known to be associated with the cancer under investigation?
   - Are there additional cases that could be related to the already identified cases?
   - Has there been an increase in the incidence rate of the cancer(s) over time?
   - How many excess cases are there?

- Are the demographic characteristics of cases unusual for the type of cancer?

4. DPHS shares conclusion and plan for next steps with the reporter and other key stakeholders (e.g., elected officials, town administrators, local health officers, etc.)

Phase III: Determine Feasibility of Conducting a Study

The purpose of this phase is to gather more information to see if it is likely that a study will show whether or not the cancer cases relate to a common cause.

1. Convene the CCRT and an expert advisory panel to review scientific literature and determine a study hypothesis based on known causes of the cancer(s) in question.
    a. Determine the plausibility that cases and contaminants could potentially be associated through:
        - Review of carcinogenicity of known contaminants,
        - Study of exposure pathways,
        - Review of historical records and
        - Gathering residential, occupational, and exposure histories for cases
    b. Identify available data on environmental contaminant(s) of concern (NOTE: It is not advisable to engage in general, open-ended inquiry to identify potential contaminants in a community, in the absence of a suspected etiologic agent).[4]
    c. Identify study design requirements and available resources to conduct a study
        i. Determine parameters to use for:
            1. Geography
            2. Timeframe that accounts for sufficient latency for cancer(s) of concern
            3. Demographics
        ii. Determine study design, sample size and statistical tests needed to test for associations
        iii. Assess resource implications and identify sources of funding
    d. Identify parameters of the proposed study including developing a case definition, methods for identification of controls which are not affected by cancer (if indicated based on proposed study design), and feasibility and methods for obtaining data from participants
    e. Determine what information (e.g., demographics, health, and risk factors) needs to be collected from cases
    f. Explore the willingness of people to participate in interviews for gathering data, particularly with potential questions about individual behaviors and other personal details

2. Convene a Community Advisory Group (CAG) to learn what the community needs and wants with regard to the investigation and set expectations around the process and potential outcomes.

3. DPHS shares conclusions of the feasibility study with the CAG and broader public plans for next steps. After discussions with the CAG, DPHS will make a determination about whether further study is warranted and feasible, but at a minimum, the following actions will be conducted:
    a. Post completed cluster investigations to the DPHS website and update chart
    b. Perform routine surveillance calculating five-year cancer rates annually using the most available NHSCR data for the specific cancer of concern. The need for annual surveillance will be evaluated on an annual basis.

[4] Centers for Disease Control and Prevention (CDC). Investigating Suspected Cancer Clusters and Responding to Community Concerns: Guidelines from CDC and the Council of State and Territorial Epidemiologists. Morbidity and Mortality Weekly Review September 27, 2013; 62(RR08); 1-14.

Phase IV: Conduct a Study

The purpose of this phase is to find out if it is likely that exposure to a specific risk factor or chemical in the environment might relate to the suspected cancer cluster.

1. The CCRT convenes to develop the study protocol. The design and components of such studies tend to be unique and will be based on circumstances and available resources

2. The CCRT conducts the study based on a developed protocol and then summarizes findings

3. Study summary and findings are publically disseminated as appropriate and will be posted on the DHHS website.